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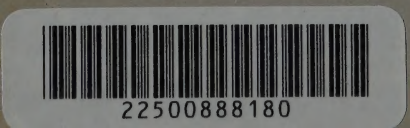

PIGMENTED ATROPHY OF THE MUCOUS MEMBRANE OF THE SMALL INTESTINE OF MALARIAL ORIGIN.

By Leonard Rogers, M.D., M.R.C.P., I.M.S., *Officiating Professor of Pathology, Medical College, Calcutta.*

(Plates XI. and XII.)

In 1897,[1] in my report on the epidemic malarial fever of Assam or Kala-agar, I gave a brief account of a chronic form of diarrhœa occurring very frequently in the cachectic stage of this intense form of malaria, and characterised, post-mortem, by a finely-dotted pigmentation and thinning of the mucous membrane of the small intestine. At a later date, on cutting sections of the intestines of these cases, I found most remarkable changes; but, unfortunately, lost all my drawings and material before publishing my observations. During the last two years I have been able to examine the bowel, microscopically, in a number of cases of chronic malarial infection, and in a few acute ones, with the result that my earlier results have been confirmed; and as the lesion has proved to be a very common and marked one in these cases, and appears to be a very important factor in producing the high mortality of malarial cachectic cases, I propose, in the present paper, to describe the changes met with.

Frequency of the Lesion in Cases of Malarial Cachexia.

In a recent paper,[2] I tabulated the naked-eye and microscopical pigmentation of the liver, spleen, and small intestines in twenty consecutive cases of fatal malarial cachexia met with in the post-mortem room of the Medical College, Calcutta. In fourteen out of the twenty cases naked-eye pigmentation of the mucous membrane of the small intestine was observed; in seven of these it was present in a marked degree, producing a dark slaty colour of the membrane, such as is illustrated in Plate XI. Fig. 1. In ten of the twenty cases sections were made; and in nine of them the black pigment of malaria

[1] "Report on the Epidemic Malarial Fever of Assam and Kala-agar, 1897."

[2] *Indian Med. Gaz.*, Calcutta, Nov. 1902.

was demonstrated in the tissues of the mucous and submucous coats of the bowel, including two cases in which no naked-eye changes had been detected, and it has since been found in several other cases, as well as in some very acute malarial infections. This is not surprising, as the parasites of malaria must sometimes lodge in the intestinal mucous membrane; but the marked cirrhosis and atrophy which accompany chronic forms of this pigmentation, leading to extreme degrees of destruction of both the villi and tube glands, and blocking the lymphatics of the submucous layer, do not yet seem to have attracted the notice which they deserve, and to these I particularly desire to draw attention.

Changes found in Death from Acute Malarial Fever.

Although the great majority of deaths caused by malaria in Lower Bengal take place after repeated attacks of fever have produced the typical familiar cachexial condition, cases are not unfrequently met with, especially in the autumn months, in which the patients are carried off by a very acute attack of malarial fever, often accompanied by cerebral symptoms, and in which malarial parasites of the malignant tertian variety are found in very large numbers in the blood. In these cases little or no naked-eye change is found in the mucous membrane of the small intestine, except sometimes a slight degree of congestion and catarrh with excess of mucous secretion, and perhaps a greyish tinge in its colour. If sections of the jejunum be cut, the appearances shown in Plate XII. Fig. 2 are met with; this specimen has been obtained from just such a case, in which the spleen was black throughout, and the liver of a dark slaty tinge, both containing a large amount of fine black pigment, while smears of the spleen pulp showed innumerable malignant tertian parasites, in all stages, from rings up to sporulating forms and crescents. In Plate XII. Fig. 2, then, we see the earliest changes produced by acute malarial infection on the mucous membrane of the small intestine, and it will be noted that it is only the villi which show any marked pathological change, the tube gland epithelium staining well, and presenting no evidence of degeneration. The villi, however, show a very large amount of dark pigment within them, and in several places this is grouped in small circles just as if it were in parasites, although some of the patches of pigment are far too large to have been derived from a single parasite, so that it is clear that a very large number of malarial organisms must have lodged in these villi in order to have produced the changes depicted. This is the only marked change met with in this acute stage, but it is evident that the blocking up of the blood and lymph vessels of such delicate structures as the intestinal villi, with anything like the amount of pigment here shown, must very materially damage them and greatly interfere with their action as

absorbents of the products of digestion. When, further, such a process is repeated day after day for months at a time, it is not surprising that the more advanced changes about to be described should ultimately result, for it is well known that the much less delicate structures of the spleen and liver undergo a marked amount of damage and fibrosis as a result of long-continued malarial irritation, by the lodgment of malarial parasites and pigment, producing the greatly thickened fibrous trabeculæ in the spleen and a greater or less degree of portal cirrhosis in the case of the liver, with much pigment in their lymphatic channels. Such a fibrosis of the spleen is always met with in chronic malaria, and some degree of the same change in the liver is much more common than appears to be generally acknowledged, while a severe degree of malarial cirrhosis of this organ, accompanied by dropsy, is by no means very rare in Calcutta.

Naked-Eye Changes in Typical Cases.

Passing on to the stages in which a typical pigmented atrophy or cirrhosis of the intestinal mucous membrane is found in chronic malarial fevers, the naked-eye changes are of a striking character, as is well illustrated in the very marked case from which Plate XI. Fig. 1 was drawn, the small piece of bowel depicted being from about the middle of the jejunum. The dark slaty-grey colour of the mucous membrane at once attracts attention, and, on observing it closely, it is found to be caused by innumerable closely-set, very fine, black points, which at once distinguishes it from any post-mortem or drug staining. This discoloration is found both on the rugæ and between them, although it tends to be darkest on the raised parts of the mucous membrane. It is always more marked in the jejunum than in the ileum; this is possibly due to the greater thickness of the mucous membrane of the upper part of the bowel, but in well-marked cases it extends throughout the whole of the small intestine. The Peyer's patches sometimes stand out as lighter areas surrounded by the pigmented portion of the bowel; but this is not always the case. The lymphatic glands of the mesentery are also darkly pigmented in typical advanced cases, or of a darkish-grey tinge in slighter degrees of this change. The stomach, as a rule, shows little naked-eye change, although in one extreme case of the affection, met with in Assam, its mucous membrane also showed very marked, finely-dotted pigmentation, exactly similar to that just described as occurring in the small intestine. The large intestine may also occasionally exhibit the change in a minor degree. Another important feature to be noted is the frequency with which the mucous membrane of the small bowel shows marked thinning and atrophy and is smoother than normal, the folds being less evident, a change the reason for which will be seen immediately.

Early Microscopical Changes in the Intestinal Mucous Membrane in Chronic Malaria.

The slighter degrees of the above-described changes present, on microscopical examination, the condition depicted in Plate XII. Fig. 3, which shows the stage of early pigmentation and cellular infiltration before marked atrophy of the mucous membrane has been produced. Considerable structural alterations are found in the mucous coat already. The villi now show, in addition to the deposits of black pigment in them, a considerable degree of thickening and distortion produced by a cellular infiltration, apparently caused by the irritating properties of the deposited pigment. Some of the villi show thickening or clubbing of their ends, others are bent down and kinked, while many are stunted and shortened, and in places have almost disappeared. Not less striking and important are the changes in the deeper layers of the mucous membrane, for it will be seen that the tube glands have nearly disappeared, leaving only their deepest portions, while their place is largely taken by a dense cellular infiltration with fine grains of dark pigment scattered throughout. The submucous coat also shows a considerable degree of pigment in larger, if more widely distributed, masses, some of which appear to be lying in the lymphatic channels. On the other hand, the muscular layers show little or no change. In such a case as that now under consideration, a number of sections may be examined without a trace of anything like a healthy piece of mucous membrane being found, the portion illustrated being fairly typical of the whole. The degree of loss of absorptive and secretory power of such a membrane can readily be imagined; but at this stage there is a possibility of considerable regeneration of the membrane, should the malarial fever finally cease; for there are sufficient epithelial cells of the tube glands left to allow of their being renewed, while many of the villi are not yet too much damaged to allow of their regaining their functions to a considerable extent; while the pigment may be carried off by the lymphatics and lodged in the nearest glands or in the submucous coat of the bowel, where it may lie without doing much harm. Such is not the case, however, with the more advanced changes next to be described.

The Advanced Cirrhotic and Atrophic Stage.

In cases of long-continued and recurring malarial fevers, going on to the condition of cachexia, still more marked alterations are met with in the intestinal mucous membrane. Instead of the cellular infiltration of the villi and deeper layers of the mucous membrane clearing up, it goes on to form fibrous tissue, with its inevitable tendency to contract, and ultimately the condition depicted in Plate XII. Figs. 4 and 5 results, the former showing the changes under the low power,

and the latter being from the same specimen under a higher magnification. The mucous membrane is now only, with some difficulty, recognised as that of the small intestine, as the villi have completely disappeared, only a few stunted remains being seen here and there on the surface of the specimen, while the tube glands are similarly only represented by a few scattered deeper portions, and indeed are not rarely found to have completely disappeared from whole fields of the microscope. Dark pigment may still be seen in greater or less amount, usually being more scanty than in the case shown in Plate XII. Figs. 4 and 5, which are from an unusually good specimen. It is now seen to be well marked throughout the whole thickness of the mucous and submucous coats, and does not preponderate so markedly in the villi. In Plate XII. Fig. 5 its distribution along the lymphatic channels of the submucous coat is well seen, while it is also found to a less extent in those between the bundles of muscular fibres; and in such a case it will be present in large amount in the mesenteric lymphatic glands. The mucous coat is much thinned in this stage, while its functions, both absorptive and secretory, must be very greatly interfered with; the extreme wasting, which is so marked a feature of malarial cachexia, thus receiving a ready explanation. Moreover, drugs as well as food may find a difficulty in entering the system when administered by the mouth; and the failure of quinine to influence the fever in many such cases, when thus given, is not surprising, and its much more powerful action when administered hypodermically also can easily be understood. An intractable form of diarrhœa occurs in advanced cases of this affection, and if it is well marked, recovery rarely takes place. I have suggested elsewhere[1] that the low secondary fever without parasites in the blood, which occurs in some cases of malarial cachexia, may possibly be brought about by this condition, through the thinned and greatly altered mucous membrane losing its selective action over the absorption of the products of digestion, and so allowing an excess of toxic bodies to enter the portal circulation, which the already enfeebled and diseased liver may be powerless to totally exclude from reaching the general circulation, and there causing slight fever, such as also often occurs in pernicious anæmia. Whether this is so or not, there can be no doubt that the nutrition of a patient affected by this intestinal pigmented atrophic cirrhosis of the intestinal mucous membrane must suffer very materially, and thus greatly decrease his powers of resistance to the organisms of pneumonia, dysentery, cancrum oris, etc., which diseases so often supervene and terminate cases of malarial cachexia; so that, directly or indirectly, the condition above described is a most important and serious complication of chronic malarial disease, and must be taken into account in the pathology of this protean disorder, and carefully remembered, more especially

[1] *Transactions of the Nagpur Malarial Convention*, 1902.

in relation to the dieting and drug treatment of cases in which it may be suspected.

DESCRIPTION OF PLATES XI. AND XII.

PLATE XI.

FIG. 1.—Naked-eye appearances in well-marked case of malarial pigmented atrophy of the mucous membrane of the small intestine.

PLATE XII.

FIG. 2.—Earliest stage of the affection, showing marked pigmentation of the villi only,—from an acute case of malarial fever. Zeiss, Objective D, Ocular 4.

FIG. 3.—Fairly early stage, showing marked cellular infiltration and pigmentation of both the villi and intertubular deeper layers of the mucous coat. Zeiss, Objective A, Ocular 4.

FIG. 4.—Advanced cirrhotic and atrophic stage under low power, showing very marked pigmentation and atrophy of both the villi and tube glands, with great excess of fibrous tissue. Zeiss, Objective A, Ocular 2.

FIG. 5.—Same as Fig. 4, but seen under higher power. Note the blocking of the lymphatics and submucous coat with masses of pigment. Zeiss, 4 D, Ocular 2.

The specimens were lightly stained with hæmatoxylin and eosin, except No. 2, which is more darkly stained with the same stains.

Fig. 1.

Fig. 2.

Fig. 3.

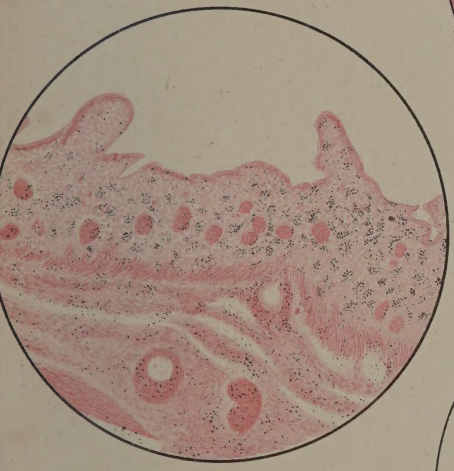

Fig. 4.

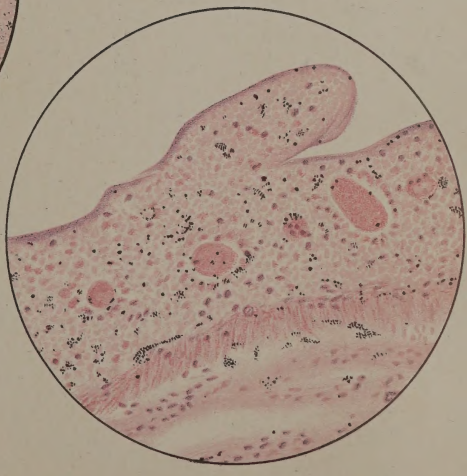

Fig. 5.